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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,302	PORRO ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	mdf

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-6,16,17,22,23 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-15,18-21 and 24-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/30/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 10/11/2005. Claims 1-35 are pending.

Election/Restrictions

Applicant's election without traverse of Group III (claims 8-34) in the reply filed on 10/11/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-6 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 16-17 and 22-23 were not examined as they are drawn to nonelected species. Election was made **without** traverse in the reply filed on 10/11/2005.

The requirement is still deemed proper and made FINAL.

Specification

The disclosure is objected to because of the following informalities: line 24 of page 7; lines 4, 11, 21 & 31 of page

8; and lines 10-11 of page 9 recite "were grown on mineral medium (2% glucose, 0.67% YNB)" and should recite "minimal medium."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-10, 18-21, 25-26, 31 & 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-10 recite "*K. lactis*". Claims 9-10 are vague and indefinite in that it is unclear if Applicant intends *Kluyveromyces lactis* or *Kloeckera lactis* or both.

Claims 9-10, 19-21, and 26 recite "*S. cerevisiae*". Claims 9-10 are vague and indefinite in that it is unclear if Applicant intends *Saccharomyces cerevisiae* or *Schizosaccharomyces cerevisiae* or both.

Claims 18 and 25 recite "linked to a promoter active in the yeast". Claims 18 and 25 are vague and indefinite in that the

metes and bounds of active are unclear. Does an "active" promoter encompass repressible promoters, inducible promoters, as well as constitutive promoters as long as they are capable of activation in yeast or do promoters "active" in yeast have a particular structural feature?

Claims 20-21 recite "*A. thaliana*". Claims 20-21 are vague and indefinite in that it is unclear whether Applicant intends *Arabidopsis thaliana*, *Aureobasidium thaliana* or both.

Claims 20-21 recite "*R. norvegicus*". Claims 20-21 are vague and indefinite in that it is unclear which genus of *R. norvegicus* is encompassed: *Rhodotorula* or some other genus?

Claim 31 recites "[t]he method of claim 7, wherein the recombinant yeast accumulates L-ascorbic acid in the medium at levels greater than background" in lines 1-2. Claim 31 is vague and indefinite in that it is unclear what is meant by "levels greater than background," i.e. do levels greater than background encompass levels of intracellular as well as extracellular levels of ascorbic acid produced above non-transformed wild-type species as determined in the examples and figures or may any detection method and any control be used to determine "levels greater than background"?

Claim 34 recites "[a] method of stabilizing ascorbic acid in a medium, comprising: culturing a yeast in the medium" in

lines 1-2. Claim 34 is vague and indefinite in that it is unclear what is meant by "stabilizing ascorbic acid": would ascorbic acid break down in the absence of cultured yeast or is the ascorbic acid stabilized in some other manner?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12-14 are drawn to recombinant yeast capable of converting an ascorbic acid precursor into L-ascorbic acid, wherein the yeast is functionally transformed with a set of D-arabinono-1,4-lactone oxidase (ALO) sequences of SEQ ID NOS: 5 & 7 (amino acid sequences of claims 12-13) and SEQ ID NOS: 6 & 8

(nucleic acid sequences of claim 14) as well as enzymes/nucleic acids having at least about 70% similarity and/or identity with those sequences. Thus the claims comprise a set of coding regions/amino acids defined by the function of the encoded protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification discloses two nucleic acid sequences and two protein sequences for ALO which have been isolated from *Saccharomyces cerevisiae* (see page 19, lines 10-15; claims 12-14; and SEQ ID NOS: 5-8 of the sequence listing). No description is provided of any other ALO sequences that result in a functionally transformed yeast cell capable of converting an ascorbic acid precursor into ascorbic acid. Neither is any description provided of any structure or sequence motifs that such ALO sequences would share. It is not even clear from the specification what the difference(s) between the two ALO sequences is(are).

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of at most two ALO enzymes from one source (*S. cerevisiae*). The results are not necessarily predictive of any other ALO sequence. Thus, it is impossible for one to extrapolate from the one nucleic acid and the one amino acid sequence described herein those sequences that would necessarily meet the structural/functional characteristics of the rejected claims.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of ALO enzymes with even 95% or 98% similarity or identity. An article published after the effective filing date of the instant application describes ALOs only from two species: *S. cerevisiae* and *Candida albicans* (Sauer, M. et al, Production of L-Ascorbic Acid by Metabolically Engineered *Saccharomyces cerevisiae* and *Zygosaccharomyces bailii*, Applied and Environmental Microbiology 70(10):6086-6091, 2004). Thus the prior art seems only to identify one additional ALO enzyme to those described in the specification.

Given the very large genus of sequences encompassed by the rejected claims, and given the limited description provided

by the prior art and specification with regard to their common sequence motifs/structures, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of ALO sequences with 70% identity and/or similarity with SEQ ID NOS: 5-8. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those embodiments that satisfy the functional limitations of the claimed genus of ALO enzymes with regard to their capability to convert ascorbic acid precursors into ascorbic acid as ALO does. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 12-14.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van

Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7—14, 18-21 and 24-33, are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1-15 of US Patent No. 6,630,330 as follows: instant claims 7-9 & 33 over patented claim 1; instant claim 10 over patented claim 2; instant claims 11-14 over patented claim 8; instant claim 18 over patented claim 11; instant claim 19 over patented claim 12; instant claims 20-21 over patented claim 9; instant claim 24 over patented claim 13; instant claim 25 over patented claim 14; instant claim 26 over patented claim 15; instant claim 27 over patented claim 10; instant claim 28 over patented claim 3; instant claim 29 over patented claim 4; instant claim 30 over patented claim 5; instant claim 31 over patented claim 6; instant claim 32 over patented claim 7. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double

patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). The MPEP states, at §804, that

> [t]he specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCOA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-2, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According o the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

With respect to instant claims 7-14, 18-21 and 24-31, an obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference

claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims(s). Although the conflicting claims are not identical, they are not patentably distinct from each other because, in the case of instant claims 7-14, 18-21 and 24-31, they are generic to all that is recited in the respective claims of the copending application, i.e., the patented claims fall entirely within the scope of each of instant claims 7-14, 18-21 and 24-31.

Claims 7 and 11-14 are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 12-14 of US Patent Application No. 10/606,300 as follows: instant claims 7 and 11-12 over co-pending claim 12; instant claim 7, 11 and 13 over co-pending claim 13; instant claims 7, 11 and 14 over copending claim 14. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s).

With respect to instant claims 7 and 11-14, the instant claim in each instance includes embodiments supported within the co-pending claims 12-14 and the portion of US Patent Application 10/606,300 that supports each of claims also defines the co-pending invention. Thus, the method of instant claims 7 and 11-14 are not patentably distinct from that of copending claims 12-14.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-8, 28, 31-32 & 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Roland et al (WO 85/0175, see entire document; IDS Reference B4).

Applicant's invention is drawn to a method of generating ascorbic acid comprising obtaining a recombinant yeast capable of converting an ascorbic acid precursor into ascorbic acid, culturing the recombinant yeast in a medium comprising an ascorbic acid precursor, thereby forming the ascorbic acid and

isolating the ascorbic acid (claim 7). The invention is further drawn to such a method wherein the yeast belongs to the genus *Saccharomyces* (claim 8), and wherein the ascorbic acid precursor is selected from D-glucose, L-galactono-1,4-lactone, L-gulono-1,4-lactone or L-galactose (claim 28). The invention is further drawn to such a method wherein the recombinant yeast accumulates L-ascorbic acid in the medium at levels greater than background and wherein the isolating step comprises chromatography (claims 31-32). Applicant's invention is further drawn to a method of stabilizing ascorbic acid in a medium, comprising culturing a yeast in the medium (claim 34).

Roland et al teach a method of generating ascorbic acid comprising obtaining a recombinant *Saccharomyces* yeast capable of converting an ascorbic acid precursor into ascorbic acid, culturing the recombinant yeast in a medium comprising an ascorbic acid precursor and isolating the ascorbic acid (see entire document, especially page 4, lines 9-13 and 28-34; page 5, lines 1-4 and 11-18: and page 39, lines 5-9). Roland et al teach this method wherein the ascorbic acid precursor is selected from L-galactono-1,4-lactone, D-glucose, L-gulono-1,4-lactone or L-galactose (page 7, line 18-23). Roland et al teach such a method wherein the recombinant yeast accumulates ascorbic acid in the medium at levels greater than background (see page

5, lines 28-34) and wherein the isolating step comprises ion exchange resin separation (page 13, line 21; and page 24, lines 15-20). Roland et al also teach a method of stabilizing ascorbic acid in a medium, comprising culturing a yeast in the medium (see page 14, lines 4-7).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 7-8, 28-32 & 34 are rejected under 35 U.S.C. 102(e) as anticipated by Berry et al (US Patent Application Publication US 2002/0012979 A1; IDS Ref. A1, see entire document).

Applicant's invention is drawn to a method of generating ascorbic acid comprising obtaining a recombinant yeast capable of converting an ascorbic acid precursor into ascorbic acid, culturing the recombinant yeast in a medium comprising an ascorbic acid precursor, thereby forming the ascorbic acid and isolating the ascorbic acid (claim 7). The invention is further

drawn to such a method wherein the yeast belongs to the genus *Saccharomyces* (claim 8), wherein the ascorbic acid precursor is selected from L-galactono-1,4-lactone; D-glucose; L-gulono-1,4-lactone; or L-galactose (claim 28), wherein the isolating step comprises lysing the yeast (claim 29), and wherein the isolating step comprises centrifugation or chromatography or crystallization (claim 30). The invention is further drawn to such a method wherein the recombinant yeast accumulates L-ascorbic acid in the medium at levels greater than background and wherein the isolating step comprises chromatography (claims 31-32). Applicant's invention is further drawn to a method of stabilizing ascorbic acid in a medium, comprising culturing a yeast in the medium (claim 34).

Berry et al teach a method for generating ascorbic acid using a genetically modified plant or microorganism, including yeast (see page 3, paragraph 33; page 4, paragraph 36; as well as page 83, claim 58), culturing the cells in a fermentation medium comprising an ascorbic acid precursor (see pages 3-4, paragraphs 33-34; as well as page 15, paragraph 117), and isolating the ascorbic acid (see page 16, paragraph 123). Berry et al also teach the method of generating ascorbic acid using a recombinant yeast of the genus *Saccharomyces* (page 2, paragraph 13) wherein the ascorbic acid precursor is D-glucose (page 15,

paragraph 116 as well as Figure 1A) and wherein the isolating step comprises lysing the yeast (page 17, paragraph 128). Berry et al further teach a method for generating ascorbic acid as above, wherein the yeast accumulates the L-ascorbic acid in the medium (see page 17, paragraph 126) and wherein the ascorbic acid is isolated utilizing chromatography or crystallization (ibid). Furthermore, Berry et al teach a method for culturing microorganisms at low pH such that extracellular ascorbic acid which is produced by the microorganism is "relatively stable" because the rate of oxidation of ascorbic acid in the fermentation medium by oxygen is reduced (see page 16, paragraphs 122-123). Berry et al teach that otherwise ascorbic acid stability can be achieved by "control of the oxygen content to very low levels to avoid oxidation of ascorbic acid" (ibid).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-9, 11-15, 18, 20-21, 24 & 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (Applied and Environmental Microbiology 65(10):4685-4687, 1999; IDS Reference C18) in view of Huh et al (Molecular Microbiology 30(4):895-903, 1998; IDS Reference C19).

Applicant's invention is drawn to a method of generating ascorbic acid comprising obtaining a recombinant yeast capable of converting an ascorbic acid precursor into ascorbic acid, culturing the recombinant yeast in a medium comprising an ascorbic acid precursor and isolating the ascorbic acid (claim

7). Applicant's invention is further drawn to such a method wherein the yeast belongs to the genus *Saccharomyces* (claim 8) and wherein the yeast belongs to the species *cerevisiae* (claim 9). The invention is further drawn to the method of claim 7, wherein the yeast is functionally transformed with a coding region encoding a first enzyme, ALO (claims 11 and 15), wherein the ALO has at least about 70% identity or similarity with SEQ ID NO:5 or SEQ ID NO:7 (claims 12-13), wherein the coding region encoding ALO has at least about 70% identity with SEQ ID NO:6 or SEQ ID NO:8 (claim 14), wherein the coding region is linked to a promoter active in the yeast (claim 18), and wherein the coding region encoding ALO was isolated from *S. cerevisiae* (claims 20-21). The invention is further drawn to a method of generating ascorbic acid wherein the yeast is functionally transformed with a coding region coding for a first enzyme, ALO, and wherein the yeast further comprises at least one coding region encoding an enzyme associated with the conversion of a carbon source to L-galactose (claim 27). Applicant's invention is further drawn to the method of claim 7 wherein the ascorbic acid precursor is selected from L-galactono-1,4-lactone; D-glucose; L-gulono-1,4-lactone; or L-galactose (claim 28), wherein the isolating step comprises lysing the yeast (claim 29) and wherein the isolating step further comprises centrifugation, filtration,

microfiltration, nanofiltration, liquid-liquid extraction, crystallization, enzymatic treatment with nuclease or protease, or chromatography (claims 30 and 32).

Lee et al teach a method of generating L-ascorbic acid with a genetically modified microorganism that is functionally transformed with a coding region encoding ALO (see entire document, especially Figure 3 and paragraph bridging pages 4686 and 4687). Lee et al teach this method wherein the microorganism is incubated in the presence of the ascorbic acid precursor, L-galactono-1,4-lactone (ibid). Lee et al teach this method wherein the ALO was isolated from *S. cerevisiae* (see page 4685, 2nd column). Lee et al teach that coexpression of another sugar dehydrogenase may give the most useful system for ascorbic acid production (see page 4687, last paragraph). Lee et al also teach the isolation of the ascorbic acid comprising lysing the microorganism and further comprising chromatography (page 4686, Figure 3).

Lee et al do not teach this method specifically utilizing a recombinant yeast. Neither do Lee et al teach this method, wherein the coding region is linked to a promoter active in the yeast.

Huh et al teach overexpression of ALO1 in *S. cerevisiae* wherein the ALO was isolated from *S. cerevisiae* and operably

linked to a promoter active in the yeast (see page 897, second column, first full paragraph). Huh et al teach that, like ALO from *C. albicans*, ALO from *S. cerevisiae* could also oxidize L-gulono-1,4-lactone as well as D-arabinono-1,4-lactone and L-galactono-1,4-lactone (page 899, first column, first full paragraph). Huh et al further teach that, although no ascorbic acid was detected in the cells when ALO was overexpressed, L-galactono-1,4-lactone can serve as a substrate for ALO, and yeast cells have been shown to synthesize ascorbic acid when L-galactono-1,4-lactone is added to the cell extraneously (page 899, second column, first full paragraph). "This fact", Huh et al teach, "makes it reasonable to suppose that, if L-galactono-1,4-lactone were present as a natural constituent in yeast cells, ascorbic acid would be detected in the cells." Huh et al further teach that the failure to detect ascorbic acid (in the ALO overexpressing cells) strongly suggests that L-galactono-1,4-lactone cannot be a natural constituent of yeast cells (ibid). Huh et al also teach that *S. cerevisiae* has been recognized as a good model system for understanding the biology of eukaryotic organisms.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute yeast overexpressing ALO operably linked to a promoter active in

yeast as taught by Huh et al in the method of generating ascorbic acid as taught by Lee et al because both Lee et al and Huh et al teach that it is within the skill of the art to utilize a recombinant microorganism transformed with ALO from *S. cerevisiae* to generate ascorbic acid.

One would have been motivated to use the ALO-overexpressing yeast as taught by Huh et al in the method of generating ascorbic acid as taught by Lee et al because Huh et al teach that *S. cerevisiae* has been recognized as a good model system for understanding the biology of eukaryotic organisms.

Thus, based upon the teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when substituting the ALO-overexpressing yeast as taught by Huh et al in the method of generating ascorbic acid as taught by Lee et al.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax

telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should

be directed to Walter A. Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office.)

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

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Patent Examiner
Art Unit 1636

January 4, 2006

JAMES KETTER
PRIMARY EXAMINER